ABSTRACT OF THE DISCLOSURE

The method of the invention provides novel compounds, termed acid-labile isotope-coded extractants (ALICE), for quantitative mass spectrometric analysis of protein mixtures. The compounds contain a thiol-reactive group that is used to capture cysteine-containing peptides from all peptide mixtures, an acid-labile linker, and a non-biological polymer. One of the two acid-labile linkers is isotopically labeled and therefore enables the direct quantitation of peptides/proteins through mass spectrometric analysis. Because no functional proteins are required to capture peptides, a higher percentage of organic solvent can be used to solubilize the peptides, particularly hydrophobic peptides, through the binding, washing and eluting steps, thus permitting much better recovery of peptides. Moreover, since the peptides are covalently linked to the non-biological polymer (ALICE), more stringent washing is allowed in order to completely remove non-specifically bound species. Finally, peptides captured by ALICE are readily eluted from the polymer support under mild acidic condition with high yield and permit the direct down stream mass spectrometric analysis without any further sample manipulation. In combination with our novel dual column two dimensional liquid chromatography- mass spectrometry (2D-LC-MS/MS) design, the ALICE procedure proves to a general approach for quantitative mass spectrometric analysis of protein mixtures with better dynamic range and sensitivity.